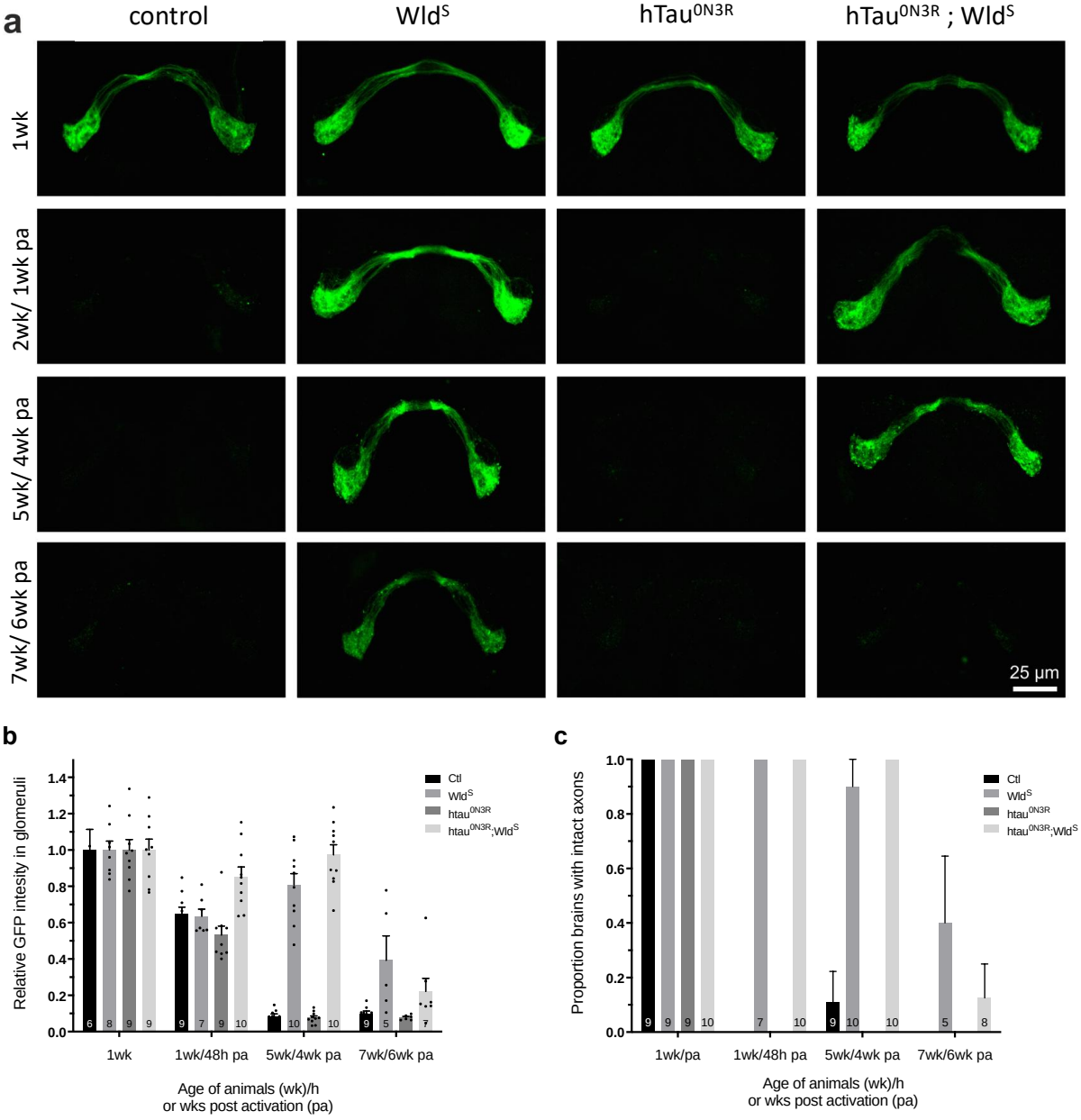
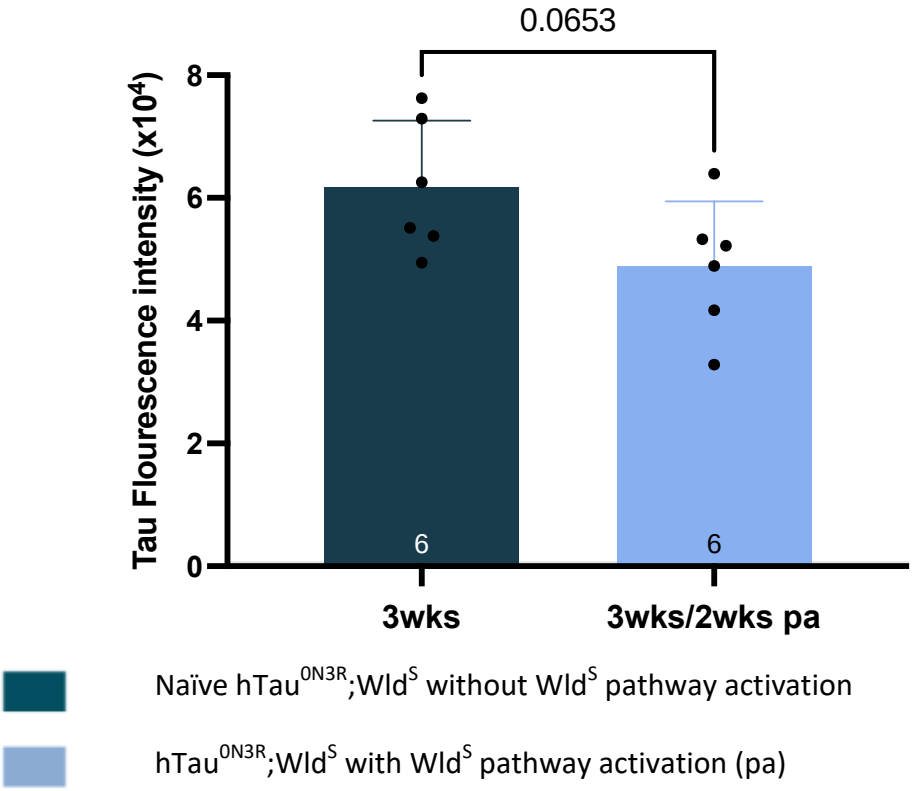
Stubbs et al Supplementary Figures

Supplementary Figure 1: Axotomy paradigm activates the pathway downstream of Wld^S as evidenced by suppression of axonal degeneration



ORNs were axotomised to activate the pathway downstream of Wld^S at 1wk post ecclosion, and brains were dissected and imaged at the indicated time points post activation (pa). At 2wk post ecclosion /1wk pa, control (ctl) and $hTau^{0N3R}$ axons have degenerated, but Wld^S and $hTau^{0N3R}$;Wld^S brains are intact. b) Measuring GFP intensity in the antennal lobe glomeruli indicates a robust delay in axonal degeneration in Wld^S brains expressing animals. c) Scoring of intact axons reveals the majority of axons expressing Wld^S, whether alone or with hTau are intact up to 5wks post ecclosion/4wk pa, but degenerate after this point. Values are presented as the mean ± SEM. n=8-14 each data point corresponds to an animal. *P<0.05, **P<0.01, ***P<0.001. (ANOVA with Bonferroni's multiple comparisons).

Supplementary Figure 2: Wld^S pathway activation does not lead to significant changes in tau levels at early time points

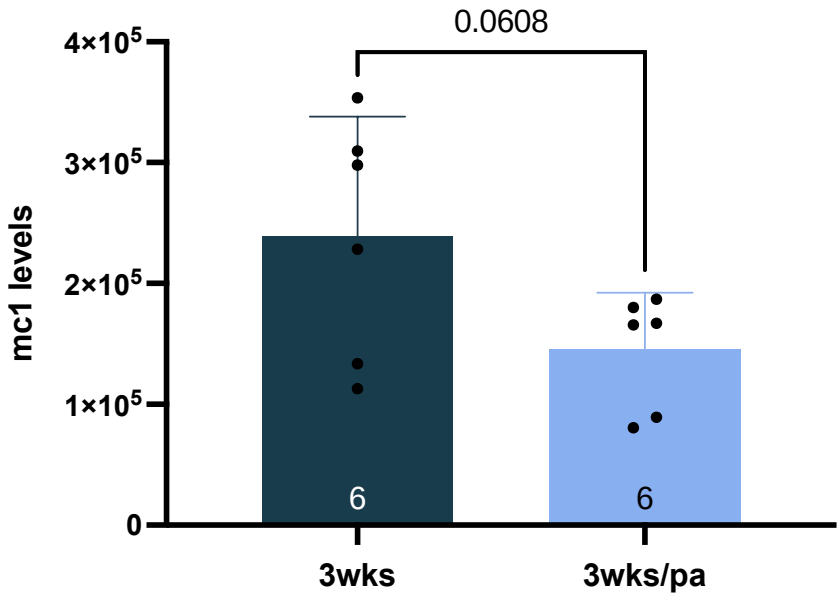


Naïve $hTau^{0N3R}$;Wld^S without Wld^S pathway activation

$hTau^{0N3R}$;Wld^S with Wld^S pathway activation (pa)

Human tau levels in 3wk $hTau^{0N3R}$;Wld^S ORNs 2wks after Wld^S pathway activation are not significantly different from those found in naïve 3wk $hTau^{0N3R}$;Wld^S ORNs that have not had Wld^S pathway activation. (n=6; each data point corresponds to an animal; p=0.07 unpaired two-tailed t test).

Supplementary Figure 3: There is a trend for misfolded tau to decrease following Wld^S pathway activation at early time points



Naïve $hTau^{0N3R}$;Wld^S without Wld^S pathway activation

$hTau^{0N3R}$;Wld^S with Wld^S pathway activation (pa)

Misfolded tau levels (probed using the MC1 antibody) in 3wk $hTau^{0N3R}$;Wld^S ORNs 2wks after Wld^S pathway activation appeared to decline compared to those found in naïve 3wk $htau^{0N3R}$;Wld^S ORNs that have not had Wld^S pathway activation. However, this trend was not significant (n=6; each data point corresponds to an animal; p=0.06 unpaired two-tailed t test).